## REMARKS

The Office Action of November 4, 2005 has been reviewed and the Examiner's comments carefully considered. Claim 92 stands rejected under 35 U.S.C. § 102(A,E2) based on supposed prior art in the Blanc et al. (the '695 patent). Claims 93-99 stand objected to but would be allowable but for their dependence on non-allowed base claim 92. Claims 100-102 also stand rejected based on their dependence on claim 92. Applicant continues to reserve the right to file, at a later time, a divisional application directed to the subject matter of non-elected claim 80.

Claim 92 has been amended by the addition of the phrase "of the same region" to indicate that the polypeptides are encoded in overlapping, or partially overlapping regions of the polynucleotide. This meaning was implicit in the unamended claim but is now made explicit. We note that the term "region" is used in this sense in a number of places in the specification.

Examiner is reminded that claims 92 through 102 were accepted in full in the *Ex parte Quayle* action of March 29, 2005, and that this acceptance was rescinded solely because of prior art elements of the '695 patent.

However, we respectfully submit that the '695 patent does not anticipate claim 92, or any claim dependent on claim 92, and the following explanation establishes why the newly cited Blanc et al. '695 patent does not anticipate or make obvious the present invention, as claimed.

The Office Action asserts that step a) of claim 92 is anticipated by Example 1, column 9, lines 30-62 and Example 6, column 39, lines 45-51 of the '695 patent. However, Example 1 of the '695 patent describes the isolation of total genomic DNA from mycelia of the organism *S. pristinaespiralis*, and does not describe the isolation or provision of a polynucleotide with a defined sequence. Example 6 describes the isolation of cosmids from a library made from genomic DNA that contain a gene of interest for which the sequence is unknown – indeed the motivation for isolating the cosmids is stated to be "in order to be able to deduce subsequently

the nucleic acid sequence of the genes identified." Accordingly, the '695 patent does not anticipate or make obvious step a) of claim 92, which requires "providing a polynucleotide having homology to a defined DNA sequence."

Nor is step c) of claim 92 anticipated by Examples 5.1.1.B and 5.1.2 of the '695 patent. Example 5.1.1.B describes the purification of the enzyme pristinamycin IIA synthase from whole *S. pristinaespiralis* cells, and shows that the enzyme is composed of two polypeptide species of approximate molecular weights 35,000 and 50,000 Daltons. Example 5.1.2 describes the N-terminal sequencing of each of the two polypeptide species. It also describes the sequencing of an internal tryptic peptide from each polypeptide, and the synthesis of two sets of degenerate oligonucleotides that could encode a portion of each peptide. The enzyme was not expressed from a polynucleotide having homology to a defined DNA sequence, nor are the two subunit polypeptides of the enzyme encoded in different reading frames of the same DNA sequence--indeed the Example proves that they are expressed from distinct and separate genes, as one would expect. Hence, the '695 patent does not anticipate step c) of claim 92, which requires "expressing two or more polypeptides from two or more reading frames of said polynucleotide, thereby creating two or more expressed polypeptides."

Finally, the Office Action suggests that steps b), d) and e) are anticipated in column 46, lines 54-58 and 61-65, which state "[f] rames 1 and 3 correspond respectively to the proteins SnaA and SnaB isolated above as described in Example 5 and for which the cloning of the genes is detailed in Example 6." However, the terms "frame" and "frame number" as used in the '695 patent have a very different meaning than the term "reading frame" as used in the instant application. In the '695 patent, the term "frame" refers to a long open reading frame in a DNA sequence – one that might encode a natural polypeptide. This is made clear in column 46, lines 7-12, "this example illustrates how it is possible to determine the open reading frames present in the nucleotide sequences defined in example 7, and to identify the genes involved in the

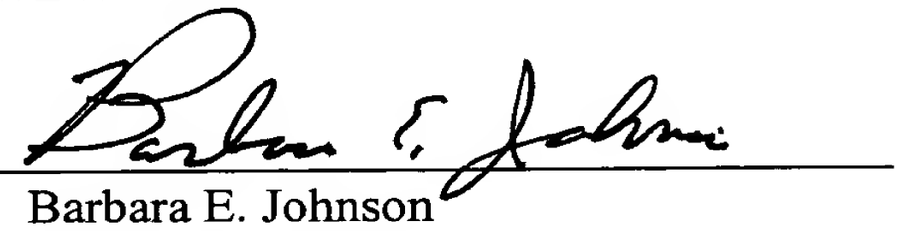
biosynthesis of pristinamycins I and pristinamycin II of *S. pristinaespiralis* SP92 as well as the polypeptides encoded by these genes," and in lines 30-39 and Table 10 of column 46: "This method [computer-based search for long open reading frames that have appropriate codon bias] enabled four highly probable open reading frames, which are shown in the following Table 10, to be characterized within the 5-kb BamHI-XhoI fragment." Inspection of Table 10 reveals that each of the four frames listed in the table occupies a separate portion of the sequence, and that none of the open reading frames overlaps another. In contrast, the term "reading frame" as used in the instant application refers to one of the six possible alternative frames in which any DNA sequence might be translated. Accordingly, the "two or more reading frames" of claim 92 are overlapping alternative translational reading frames within the same polynucleotide, whereas the different frames in the '695 patent are different non-overlapping polynucleotide sequences. Thus, step b) of claim 92 of the instant application is not anticipated by the '695 patent because the '695 patent makes no mention of polypeptides that are, or might be, encoded in overlapping reading frames of the same polynucleotide sequence. The '695 patent certainly does not teach the providing of a polypeptide as claimed in which a difference is suspected. Further, step d) of claim 92 is not anticipated because the '695 patent makes no mention of measuring the masses of two or more polypeptides expressed from overlapping reading frames of the same polynucleotide sequence. And finally, step e) of claim 92 is not anticipated by the '695 patent because the '695 patent makes no mention of comparing the predicted mass values of two or more polypeptides encoded in alternate reading frames of a polynucleotide with observed mass values of polypeptides expressed from such a polynucleotide.

## CONCLUSION

For the reasons cited above, we submit that the '695 patent does not anticipate claim 92, or any claim dependent on claim 92, and withdrawal of the rejections and allowance of claims 92-102 are respectfully requested.

Respectfully submitted,

THE WEBB LAW FIRM

By 

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